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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COPPINS, JANET L	
ART UNIT	PAPER NUMBER
1626	

NOTIFICATION DATE	DELIVERY MODE
10/09/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/566,400	MERCE VIDAL ET AL.	
	Examiner	Art Unit	
	JANET L. COPPINS	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,21-47 and 49-76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,21,35-42,44,45 and 49-74* is/are rejected.

7)☒ Claim(s) *2-19, 22-34, 43, 46, 47, 75 and 76* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-19, 21-47 and 49-76 are pending in the instant application.

Response to Amendment

2. Applicant's Amendment and Response, received April 11, 2008, has been reviewed by the Examiner and entered of record in the file. Accordingly, claims 20 and 48 have been cancelled and new claims 75 and 76 have been added.

Status of the Claims

3. Claims 1-19, 21-47 and 49-76 are pending in the instant application. Claims 10-15 and 47-74, were previously withdrawn from further consideration by the Examiner as being drawn to non-elected inventions.

4. In view of Applicants' persuasive arguments, the Examiner has expanded the scope of the invention of the elected subject matter to include all compounds according to formula (Ia) and has rejoined all claims for examination.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. (a) Claim 1 previously rejected for reciting, "…optionally in form of one of their stereoisomers, preferably enantiomers or diastereomers, their racemate or in form of a mixture of

at least two of their stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a salt thereof, preferably a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof." Applicants have still failed to designate any chiral centers, and have neglected to label any such *cis/trans* orientations or any enantiomeric rotations, therefore it is unclear which stereoisomers, or mixtures, etc. Applicants are intending to claim. The Examiner cautions that Applicants should take note when amending claim 1, since the Specification also fails to designate any geometric or optical isomers within formula I and does not indicate any chiral centers or orientations, other than a general mention on pages 10, 26, 27, etc. Therefore the rejection of claim 1 is maintained.

(b) Claim 18 previously rejected for reciting "suitable solvent." In view of Applicant's amendments, the rejection is withdrawn.

(c) Claims 19 and 20 previously rejected for reciting the term "medicament. In view of Applicant's amendatory changes to reformat the claims as methods of use, the rejection is withdrawn.

(d) Claims 21-46 previously rejected under 35 USC 112 and 35 USC 101, for reciting "the use of" a compound according to claims 1-9. In view of Applicants' amendments to delete the "use" language from the claims, the rejection is withdrawn.

The following new rejections are applied under *35 USC § 112:*

8. Claims 21, 35-42 and 44-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for treating certain diseases such as anxiety, depression, eating disorders, etc., does not reasonably provide enablement for all of the above claimed diseases. The specification fails to provide sufficient support of the broad use of the

compound of the claim 1 for regulating a 5-HT_6 receptor, or for the treatment of all claimed neurodegenerative disorders and cognitive and personality disorders of claims 35-42 and 44-46.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The specification, while being enabling for compounds according to formula (Ia) for treating certain claimed diseases that respond to the regulation of the serotonin (5-HT) receptor, does not reasonably provide enablement for treating all of the diseases listed by the above claims.

Applicants are claiming a method of treating many unrelated diseases, including diseases that are not enabled, such as Alzheimer's disease, multiple sclerosis, dementia, MS, Parkinson's, Huntington's, etc.

The nature of the invention

The nature of the invention is methods of treating inflammatory, immune, and proliferative disorders/diseases, or diseases involving the 5-HT pathways, comprising administering a compound to a patient in need thereof. The language of claims 21, 35-42 and 44-45 encompasses a "laundry list" of diseases that are unrelated and are not enabled.

The state of the prior art

The state of the prior art is that serotonin receptors of the 5-HT6 subtype are known to be implicated in diseases/disorders such as depression, anxiety, eating disorders, etc.

The predictability or lack thereof in the art

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In most instances, the etiological causes of neurodegenerative disorders are unknown. While symptomatic treatments are available for many neurodegenerative disorders, drugs to reduce or prevent the neuronal loss in patients have yet to be identified. It is the state of the art that there is no known cure or prevention for Alzheimer's disease, furthermore, there are only four medications available in the United States available to temporarily slow the early stages of Alzheimer's disease. The current drugs for the treatment of Alzheimer's disease, ARICEPT®, EXELON®, REMINYL® and COGNEX®, treat early stages of Alzheimer's disease by delaying the breakdown of acetylcholine. MEMANTINE®, which blocks excess amounts of glutamate, treats late stage Alzheimer's disease. (<URL:http://www.cnn.com/2003/HEALTH/conditions/09/24/alzheimers.drug.ap/index.html>).

Regarding the autoimmune disease MS since it can take several different forms and its exact cause remains unknown, treatment has been extremely difficult and there is currently no

cure. Likwise, Huntington's and Parkinson's are also very difficult to treat and diagnose since the course of the disease is very unpredictable and the exact causes are not known.

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment by the compound of the instant claims, one of skill in the art is unable to fully predict possible results from the administration of the compound of the instant claims.

The amount of direction or guidance present and

the presence or absence of working examples

The specification has enabled only the compounds according to formula (I) that selectively bind 5-HT. As stated previously, the efficacy of an individual compound against a specific disease or symptom needs to be specifically and individually supported by factual evidence. Such evidence has not been described or supported by the specification.

In addition, there is no proof that the claimed compounds have ever been administered to a human or to an animal model. Likewise, Applicants have not shown that the instant compounds are beneficial for treating any type of neurodegenerative or autoimmune disorder. In most instances, the etiological causes of both types of disorders are unknown. While symptomatic treatments are available for many neurodegenerative or autoimmune disorders, drugs to reduce or prevent the neuronal loss in patients have yet to be identified. The claims include disorders that are extremely difficult to treat and have no known cure, such as Alzheimer's, MS, Parkinson's and Huntington's. Currently there are no medications on the market that even slow the progress of these diseases.

The specification also only discusses an *in vitro* inhibition assay on page 41, which compares the IC_{50} values of human cell lines, yet provides no data for describing the efficacy of

the claimed compounds for treating the full scope of disorders that Applicants have recited.

The breadth of the claims

Applicants are claiming methods of treating a broad number of diseases that are unrelated. The allegation that the diseases claimed by the Applicants are all connected to the immune system or implicate the 5-HT receptor is insufficient support that the claimed compounds have specific efficacy in current available form for treating all of the diseases/disorders listed in claims 35-42 and 44-45, specifically Alzheimer's, MS, Huntington's, Parkinson's, dementia, diseases of the CNS , schizophrenia, etc.

The quantity of experimentation needed

The quantity of experimentation needed is undue. One of ordinary skill in the art without direction, would be unable to treat each and every disease/condition listed by claims 35-42 and 44-45, using the instant claimed compounds. One of skill in the art would need to determine which diseases/disorders would be benefited by modulating the 5-HT receptor and would furthermore then have to determine whether the claimed compounds would provide treatment of all of the disorders and conditions encompassed by the above claims. Based on the unpredictable nature of the invention and the state of the prior art and the breadth of the claims, one of ordinary skill in the art would be burdened with undue "experimentation study" to determine whether the claimed compounds are capable of treating Alzheimer's, MS, Huntington's, Parkinson's, dementia, diseases of the CNS, etc.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be

individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can actually be treated by the compound encompassed in the instant claims, with no assurance of success.

The Examiner recommends deleting the claims to "cognitive memory disorders," "Alzheimer's Disease," "Multiple Sclerosis," "Huntington's," "dementia" and "senile dementia processed," "disorders of the CNS," "schizophrenia," and "psychosis" and to insert specific diseases that are enabled into claim 21, i.e. incorporate "for treating a disease or disorder selected from the group consisting of…" after "A method of regulating a 5-HT_6 receptor," or insert the phrase "*in vitro*" into claim 21.

9. Claims 49-74 provide for "the use of' a compound according to claim 10, but, since the claim does not Set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

10. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claims 49-74 also rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process; i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example Ex parte Dunki, 153 USPQ 678 (Bd.App. 1967) and Clinical Products, Ltd. v. Brenner, 255 F. Supp. 131,149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

12. Claims 1 and 3-8 previously rejected under 35 U.S.C. 102(b) as being anticipated by Radl et al, Collection of Czechoslovak Chemical Communications. In view of Applicant's persuasive arguments, the anticipation rejection is withdrawn.

Claim Objections

13. Claims 4, 8, 9, 16-19 and 21-46 previously objected to under 37 CFR 1.75(c) as being in improper multiple dependent form. Applicants' amendments have corrected the dependencies, and therefore the objections are withdrawn.

14. Claims 2-19, 22-34, 43, 46, 47, 75 and 76 are objected to under 37 CFR 1.75(c) as being dependent on rejected base claims.

Conclusion

14. In conclusion, claims 1-19, 21-47 and 49-76 are pending in the instant application. Claims 1, 21, 35-42, 44, 45, and 49-74 are currently rejected, and claims 2-19, 22-34, 43, 46, 47, 75 and 76 are objected to.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JANET L. COPPINS whose telephone number is (571)272-0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/REI-TSANG SHIAO /
Primary Examiner, Art Unit 1626

Janet L. Coppins
October 1, 2008